REMARKS

Upon entry of this amendment claims 1-7 and 31-42 will be pending. Claims 2 and 5 have been amended, support for which can be found throughout the specification. No new matter has been added.

Summary of the Invention

As an initial matter as an aid to the Office in better understanding the present invention a summary is included. The present invention is directed to an isolated nucleic acid, a vector, an isolated host cell, and methods of use thereof relating to a novel DNA and protein sequence that is referred to as exon-3 deleted manganese superoxide dismutase (MnSOD E3(-)). MnSOD E3(-) is a splice variant made from the same gene that encodes the protein manganese superoxide dismutase (MnSOD) wherein the third exon that is normally present in the mRNA of MnSOD is absent. MnSOD is known to be an enzyme that has anti-oxidant activity, that is the MnSOD helps to neutralize oxidative molecules, such as, superoxide. MnSOD E3(-) also comprises enzymatic activity, however, its activity is opposite of MnSOD, in that it is pro-oxidant, that it creates oxidative molecules. Accordingly, the present invention describes a molecule (amino acid and nucleic acid), MnSOD E3(-), that although similar in sequence to MnSOD, has enzymatic activity that is completely opposite to MnSOD due to the lack of the third exon. The deletion of the third exon generates a nucleic acid sequence, SEQ ID NO: 3, that is unique to MnSOD E3(-), which encodes for the amino acid sequence SEQ ID NO: 4.

Rejections under 35 U.S.C § 112

Claims 4, 5, 40 stand rejected under 35 U.S.C § 112, first paragraph as allegedly failing to comply with the enablement requirement. The Office alleges that the claims are not enabled because the host cell described in claim 5 would encompass a cell within a living organism "such as a transgenic animal or a human gene therapy patient. It is noted that the specification contemplates gene therapy on page 26, line 27," and that the specification does not teach how to overcome problems with *in vivo* delivery and expression. (Office Action, page 3).

Applicants respectfully disagree because the claimed host cells are enabled. However, in order to further prosecution, applicants have amended claim 5 to recite "An isolated host cell"

as suggested by the Examiner. Support for this amendment can be found throughout the specification and the examples. Accordingly, Applicants respectfully request that the rejection be withdrawn.

Claims 1-6, 31, 33-35, 40, and 41 stand rejected under 35 U.S.C § 112, first paragraph, as allegedly failing to comply with the written description requirement. The Office alleges that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skill in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. As the Office states, "this is a written description rejection." (Office Action, page 5). The Office alleges that the claims are drawn to nucleic acid sequences with at least 70% or 97% homology to a sequence and that in the instant case, "other than SEQ ID 1 (552 bases to encode SEQ ID#2) no other sequences are disclosed that are 70 or 97% of the protein encoding SEQ ID#2. Thus, only the full sequence of SEQ ID#1 is described such that it can be used." (Office Action, page 5). Applicant respectfully disagrees.

Applicants have sufficiently described the invention. The M.P.E.P states:

> Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or ***by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention.***

(M.P.E.P. § 2163, emphasis added). Applicant has sufficiently described "distinguishing identifying characteristics" to show possession of the claimed invention. Applicant has described an isolated nucleic acid molecule encoding a protein comprising an amino acid sequence comprising SEQ ID NO: 2, wherein the protein has pro-oxidant activity. Applicant has also described an isolated nucleic acid molecule encoding a protein comprising an amino acid sequence comprising at least 70% sequence identity to SEQ ID NO: 2, wherein the protein has pro-oxidant activity (specification, page 9, lines 27). Applicant has described the function of the protein encoded by the nucleic acid molecule as pro-oxidant. The Applicant has also described what is meant by 70% sequence identity and how to determine the percent identity (specification, page 9). Thus, the applicant has clearly described the distinguishing characteristics of claim 1, which include both the sequence (encoding for an amino acid sequence that is 70% identical to

SEQ ID NO: 2) and function of the encoded protein (pro-oxidant). Thus, claim 1 is clearly described.

Applicant has also sufficiently described claim 2. Claim 2 states, "An isolated nucleic acid molecule comprising at least 97% identity to SEQ ID NO: 1." One of skill in the art would clearly understand that Applicant was in possession of sequences that are 97% identical to SEQ ID NO: 1. However, in order to further prosecution, Applicant has amended claim 2 to recite that the sequence also encodes a protein that has pro-oxidant activity. Thus, the claimed sequence has a specific structure and a specific function. One of skill in the art would clearly understand that Applicants were in possession of the claimed invention.

The Examiner also alleges that the specification teaches that 70% and 97% allows for "enough changes to read on the undeleted sequence and thus detect non-exon3 deleted sequences." (Office Action, page 5). As an initial matter, none of the claims in the present application refer to hybridization and therefore, whether or not the sequence could "detect" non-exon-3 deleted sequences is irrelevant to the pending claims. However, the claims comprises the element that the nucleic acid molecule must encode for a protein that has ***pro***-oxidant activity. As stated above, the nucleic acid molecule that comprises exon-3 (*i.e.* MnSOD) encodes a protein that has ***anti***-oxidant activity and a nucleic acid molecule that lacks exon-3 encodes a protein that has ***pro***-oxidant activity . One of skill in the art would understand that the Applicant was in possession of the claimed invention at the time the application was filed.

Claims 1-6, 33, 34, and 40 stand rejected under 35 U.S.C § 112, first paragraph as allegedly not providing enablement for "hybridization using sequences with homologies less than 100%." Applicant respectfully disagrees.

As can be seen from the listing of the claims contained herein none of the claims refer to hybridization. The claims to refer to percent identity, however, the specification clearly enables one of skill in the art to determine if a sequence has a certain identity and whether or not the protein encoded by the nucleic acid molecule has pro-oxidant activity. For example, the specification describes how to determine percent identity (specification, page 9) as well as determine the oxidative activity of any encoded protein, see, for example, Example 5 (specification, pages 39-40). However, one of skill in the art would readily know how to do either of these tasks without undue experimentation using only routine methods known to the skilled artisan. Accordingly, the claims are enabled.

Applicant respectfully requests that if the Examiner maintains the rejection based on "enablement for hybridization", that the Examiner more clearly explain why hybridization is relevant to the pending claims since the term is not used in any of the pending claims.

In view of the foregoing, Applicant respectfully requests that the rejections under 35 U.S.C § 112 be withdrawn.

Rejection under 35 U.S.C § 102

Claims 1, 3-6, 33, 37, 38, and 40 stand rejected under 35 U.S.C § 102(b) as allegedly being anticipated by Heckl *et al.* (U.S. Patent 5,240,847). The Office alleges that the claims are drawn to a nucleic acid sequence encoding a protein 70% identical to SEQ ID NO:2 and that the Heckl reference discusses a nucleic acid sequence that encodes a protein at least 70% identical to SEQ ID #2 and, therefore, anticipates the present invention. Applicant respectfully disagrees.

Claim 1 recites:

> An isolated nucleic acid molecule encoding a protein comprising an amino acid sequence comprising at least 70% sequence identity to SEQ ID NO: 2, ***wherein the protein has pro-oxidant activity***.

(emphasis added). For a reference to anticipate an invention, the reference must describe each and every element in the claims. The standard for anticipation under § 102(b) is one of strict identity. An anticipation rejection requires a showing that each limitation of a claim be found in a single reference. *Atlas Powder Co. v. E.I. DuPont de Nemours & Co.*, 224 U.S.P.Q. 409, 411 (Fed. Cir. 1984). The Heckl reference fails to anticipate the pending claims because it does describe or suggest a protein as described in the claims and, specifically, claim 1.

The Heckl reference describes a human manganese superoxide dismutase. As discussed above, MnSOD has ***anti***-oxidant activity, *i.e.*, it scavenges superoxide radicals. The Heckl reference ***fails to*** teach or even suggest an isolated nucleic acid molecule encoding a protein comprising an amino acid sequence comprising at least 70% sequence identity to SEQ ID NO: 2, ***wherein the protein has pro-oxidant activity***. Accordingly, the Heckl reference fails to anticipate the claimed invention.

In view of the foregoing, Applicant respectfully requests that the rejection under 35 U.S.C § 102 be withdrawn.

Objections

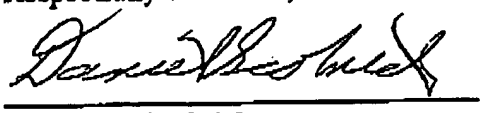
Claims 32, 36, 39, and 42 stand objected to because they depend on rejected claims, but would be allowable if rewritten in independent form. Applicant respectfully asserts that the rejection of the claims that claims 32, 36, 39, and 42 depend from are improper and will be allowed in view of the present response. Thus, the objection is believed to moot in view of the amendments and arguments made herein.

In view of the foregoing, Applicant respectfully requests that the objection be withdrawn.

Conclusion

The examination of the pending claims and passage to allowance are respectfully requested. An early Notice of Allowance is therefore earnestly solicited. Applicants invite the Examiner to contact the undersigned at (215) 665-6928 to clarify any unresolved issues raised by this response.

Respectfully submitted,



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